

Attorney Docket No. 00789-05
Patent Application Serial No. 10/517,328
Response to 9/5/06 Final Office Action

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IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

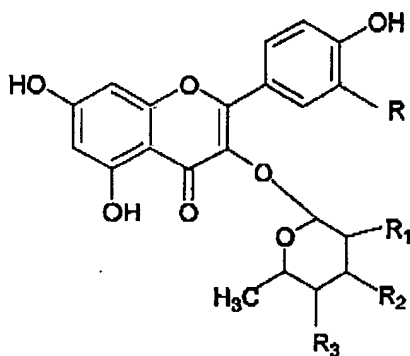
1-9 (Canceled)

10. (Withdrawn) An extract of tissues from the plant *Forsteronia refracta*, wherein said extract has Rsk specific inhibitory activity.

11. (Withdrawn) The extract of claim 10, wherein the extract is prepared by extracting tissues, selected from the group consisting of wood stem and stem bark of *Forsteronia refracta*, with a solvent comprising alcohol.

12. (Withdrawn) The extract of claim 10 wherein the extract is enriched for flavonoid compounds relative to other components present in the natural tissues.

13. (Withdrawn) A method of specifically inhibiting Rsk activity, said method comprising the step of contacting a Rsk enzyme with a compound represented by the general structure:



III

wherein R is H or OH, and R₁, R₂ and R₃ are independently selected from the group consisting of hydroxy -OCOR₄, -COR₄ and C₁-C₄ alkoxy; and
R₄ is H or C₁-C₄ alkyl.

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14. (Withdrawn) The method of claim 13, wherein R is H or OH and R₁, R₂ and R₃ are independently selected from the group consisting of hydroxy and -OCOCH₃.

15. (Withdrawn) The method of claims 13 or 14 wherein R is H.

16. (Withdrawn) The method of claims 13, 14 or 15, wherein R₃ is -OCOCH₃.

17. (Withdrawn) A method of screening for Rsk inhibitory compounds, said method comprising the steps of

contacting a Rsk substrate with Rsk and a potential inhibitory compound under conditions that are permissive for kinase activity;

incubating the substrate for a predetermined length of time; and

determining if the substrate is phosphorylated, wherein a decrease in kinase activity relative to a reaction run in the absence of said potential inhibitory compound identifies an inhibitory compound.

18. (Withdrawn) The method of claim 17 wherein the step of determining if the substrate is phosphorylated, comprises quantitating the level of phosphorylation through the use of phosphospecific antibodies.

19. (Withdrawn) A method of preparing an extract that has Rsk specific inhibitory activity, said method comprising the steps of

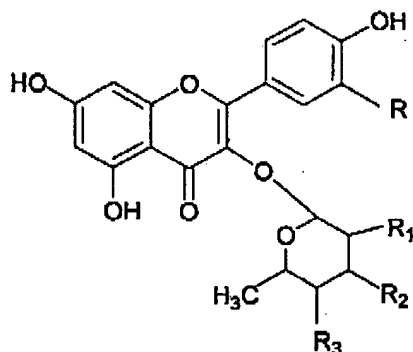
contacting *F. refracta* tissue with an alcohol solution to produce a crude extract; and

fractionating the crude extract to isolate flavonoid compounds that exhibit Rsk specific inhibitory activity.

20. (Withdrawn) The method of claim 19 wherein the tissue comprises tissue selected from the group consisting of wood stem and bark of *F. refracta* and the contacting step comprises soaking the tissue multiple times in methanol.

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21. (Currently Amended) A method for treating a ~~disease or condition~~ cancer characterized by ~~inappropriate~~ excessive Rsk activity, said method comprising the step of administering to a human or other mammal in need thereof, a composition comprising a compound represented by the general structure:



wherein R is H or OH, and R₁, R₂ and R₃ are independently selected from the group consisting of hydroxy, -OCOCH₃, -COCH₃, C₁-C₄ alkoxy, -O-glucoside and -O-rhamnoside in an amount effective for specifically inhibiting Rsk activity in the cells of said human or mammal.

22. (Original) The method of claim 21 wherein R is H and R₁, R₂ and R₃ are independently selected from the group consisting of hydroxy and -OCOCH₃.

23. (Original) The method of claim 21 wherein R is H or OH, R₁ and R₂ are independently hydroxy or -OCOCH₃ and R₃ is -OCOCH₃.

24. (Original) The method of claim 23 wherein R is H.

25. (Currently Amended) A method for treating a ~~disease or condition~~ cancer characterized by ~~inappropriate~~ excessive Rsk activity, said method comprising the step of administering to a patient in need thereof a composition comprising a Rsk specific inhibitor in an amount effective for specifically inhibiting Rsk activity.

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26. (Original) The method of claim 25 wherein the Rsk specific inhibitor comprises a compound selected from the group consisting of an anti-sense oligonucleotide and an interfering oligonucleotide.

27. (Original) The method of claim 25 wherein the Rsk specific inhibitor comprises an interfering oligonucleotide directed against Rsk1, Rsk2, Rsk3 or Rsk4.

28. (Original) The method of claim 25 wherein the Rsk specific inhibitor comprises an extract from the tissues of *Forsteronia refracta* or *Zingiber zerumbet*.

29-31. (Canceled)

32. (Currently Amended) The method of claim ~~31~~ 21 further comprising the steps of administering said ~~patient~~ human or other mammal anti-tumor therapy.

33-38. (Canceled)

39. (Withdrawn) A diagnostic method for detecting neoplastic cells, said method comprising the steps of
measuring a Rsk quantification factor, selected from the group consisting of Rsk nucleic acid quantity, Rsk protein quantity or Rsk enzymatic activity, in a biological sample isolated from an individual; and
determining if the Rsk quantification factor is elevated relative to a standard, wherein an elevated Rsk quantification factor detected in said biological sample indicates the presence of neoplastic cells.

40. (Withdrawn) The method of claim 39 wherein the biological sample comprises cells recovered from a biopsy.

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41. (Withdrawn) The method of claim 39 wherein the standard comprises a corresponding non-Rsk nucleic acid quantity, non-Rsk protein quantity or non-Rsk enzymatic activity detected in said biological sample.

42. (Withdrawn) The method of claim 39 wherein the standard comprises a corresponding Rsk nucleic acid quantity, Rsk protein quantity or Rsk enzymatic activity detected in healthy tissue of said individual.

43. (Withdrawn) The method of claim 39 wherein the standard comprises a corresponding Rsk quantification factor detected in a reference biological sample obtained from healthy tissue.

44. (Withdrawn) The method of claim 39 wherein the measured Rsk quantification factor is Rsk activity, and the step of measuring the Rsk activity comprises isolating Rsk protein from said biological sample and conducting *in vitro* kinase assays

45. (Withdrawn) The method of claim 39 wherein the measured Rsk quantification factor is Rsk protein quantity and the step of measuring the quantity of Rsk protein comprises contacting the Rsk protein with an antibody specific for Rsk protein, wherein the antibody is labeled;
removing the non-bound and non-specific antibody; and
quantifying the amount of label remaining to determine the amount of Rsk protein present.

46. (Withdrawn) The method of claim 39 wherein the measured Rsk quantification factor is Rsk nucleic acid quantity and the step of measuring the quantity of nucleic acid comprises
contacting the nucleic acids of the biological sample with a labeled Rsk complementary nucleic acid probe;
removing the non-bound and non-specific probe; and

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quantifying the amount of label remaining to determine the amount of Rsk nucleic acid present in the biological sample.

47. (Withdrawn) A composition comprising a Rsk inhibitor isolated by the steps of extracting tissues, selected from the group consisting of wood stem and stem bark of *Forsteronia refracta*, with a methanol solution;

applying the extracted material to a polyamide 6S column;

washing successively with H₂O, 1:1 H₂O-MeOH, 9:1 CH₂Cl₂-MeOH and 1:1 CH₂Cl₂-MeOH to afford four fractions;

recovering the 1:1 CH₂Cl₂-MeOH fraction;

applying the 1:1 CH₂Cl₂-MeOH fraction to a diol gel column;

washing successively with CH₂Cl₂, 99:1 CH₂Cl₂-MeOH, 95:5 CH₂Cl₂-MeOH, 90:10 CH₂Cl₂-MeOH and MeOH to give five fractions;

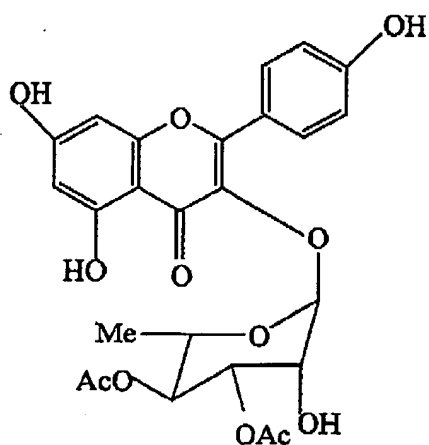
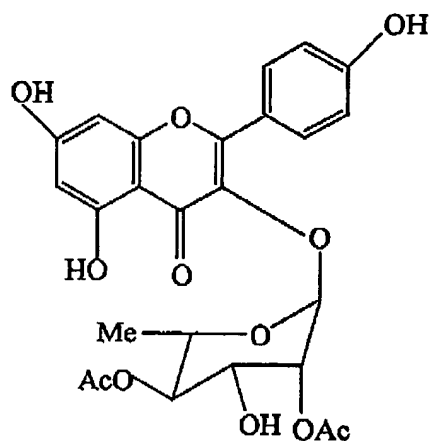
combining the 99:1 CH₂Cl₂-MeOH, 95:5 CH₂Cl₂-MeOH and 90:10 CH₂Cl₂-MeOH fractions to isolate a composition comprising a Rsk inhibitor.

48-50 (Canceled)

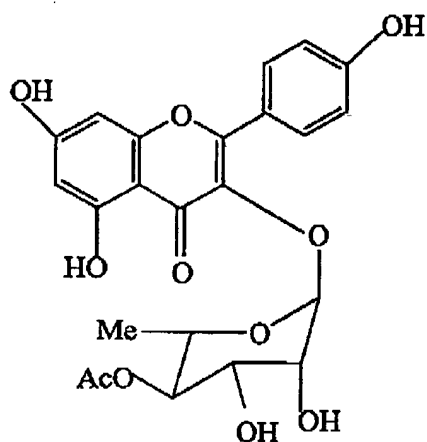
51. (New) The method of claim 21, wherein said cancer is selected from the group consisting of breast cancer, prostate cancer, and sarcoma.

52. (New) The method of claim 51, wherein said Rsk inhibitor is selected from the group consisting of SL0101-1, SL0101-2, and SL0101-3, having the following structures:

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**SL0101-1****SL0101-2**

and

**SL0101-3**

53. (New) The method of claim 25, wherein said cancer is selected from the group consisting of breast cancer, prostate cancer, and sarcoma.